

## PROCESSES FOR PREPARING CALCIUM SALT FORMS OF STATINS

### CROSS-REFERENCE TO RELATED APPLICATIONS

5        <sup>IS A DIV. OF 10/222,556 FILED 8/16/02 NOW 6,777,552,</sup>  
This application claims the benefit of provisional application Serial Number  
60/312,812, filed August 16, 2001 and U.S. Patent Application Serial No. 10/037,412,  
filed October 24, 2001, <sup>NOW 6,528,661.</sup> ~~which claims the benefit of provisional application Serial Number~~  
60/249,319, filed November 16, 2000, ~~all of which are incorporated herein by reference.~~

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10/25/04

### FIELD OF THE INVENTION

10        The present invention relates to processes for preparing calcium salt forms of  
statins.

### BACKGROUND OF THE INVENTION

15        The class of drugs called statins are currently the most therapeutically effective  
drugs available for reducing low-density lipoprotein (LDL) particle concentration in the  
blood stream of patients at risk for cardiovascular disease and thus, statins are used in the  
treatment of hypercholesterolemia, hyperlipoproteinemia, and atherosclerosis. A high  
level of LDL in the bloodstream has been linked to the formation of coronary lesions that  
20        obstruct the flow of blood and can rupture and promote thrombosis. Goodman and  
Gilman, The Pharmacological Basis of Therapeutics, page 879 (9th Ed. 1996).

25        Statins inhibit cholesterol biosynthesis in humans by competitively inhibiting the  
3-hydroxy-3-methyl-glutaryl-coenzyme A ("HMG-CoA") reductase enzyme. HMG-CoA  
reductase catalyzes the conversion of HMG to mevalonate, which is the rate determining  
step in the biosynthesis of cholesterol. Decreased production of cholesterol causes an  
increase in the number of LDL receptors and corresponding reduction in the concentration  
of LDL particles in the bloodstream. Reduction in the LDL level in the bloodstream  
reduces the risk of coronary artery disease. J.A.M.A. 1984, 251, 351-74.

30        Currently available statins include lovastatin, simvastatin, pravastatin, fluvastatin,  
cerivastatin and atorvastatin. Lovastatin (disclosed in U.S. Pat. No. 4,231,938) and  
simvastatin (ZOCOR; disclosed in U.S. Pat. No. 4,444,784 and WO 00/53566) are  
administered in the lactone form. After absorption, the lactone ring is opened in the liver  
by chemical or enzymatic hydrolysis, and the active hydroxy acid is generated.